Metastasis-promoting protein identified; could provide a prognostic test or target for breast cancer

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Tumors that are about to progress and metastasize go through a process also seen in normal embryonic development, known as the epithelial to mesenchymal transition (EMT). Tumor cells revert to a less-differentiated state, stop adhering to each another and become more mobile and prone to invade and proliferate. Now, researchers at Children's Hospital Boston show, for the first time, that a small protein called lipocalin 2 triggers the EMT in human breast cancer - and that the same protein, when measured in tissues and urine, can predict a cancer's invasiveness. Their findings were published online February 23 by the *Proceedings of the National Academy of Sciences*.

Researchers led by Marsha A. Moses, PhD, and Jiang Yang, PhD, of the Vascular Biology Program at Children's, induced human breast cancer cells to make large amounts of lipocalin 2, and showed that cell motility and invasiveness increased significantly. They then took cells from aggressive breast cancers and silenced lipocalin 2, and found that cell migration was significantly inhibited. When they transplanted human breast cancer cells into animals, those from tumors making lipocalin 2 were more locally invasive and more likely to metastasize to lymph nodes.

Further laboratory studies indicated that lipocalin 2 decreases the levels of estrogen receptor alpha, thereby reducing the cells' response to the hormone estrogen, which is associated with poor prognosis of breast

cancer. Inhibiting the production of estrogen receptor alpha is also the mechanism that triggers the EMT pathway, the researchers show.

Finally, tissue samples, and even urine samples, from women with invasive breast cancer consistently showed elevated lipocalin 2 levels, suggesting that testing for lipocalin 2 may be a way of detecting cancer progression and the need for more aggressive treatment.

"Our study identifies a novel, additional player in the complex development of invasive breast cancer," says Moses, the Vascular Biology Program's interim director. "It suggests that this protein may represent a prognostic and/or therapeutic target for this devastating disease."

Source: Children's Hospital Boston